CANADIAN JOURNAL OF RESEARCH

VOLUME 22 JUNE, 1944 NUMBER 3

— SECTION E —

MEDICAL SCIENCES

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OTTAWA, CANADA

CANADIAN JOURNAL OF RESEARCH

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The *Canadian Journal of Research* is published by the National Research Council of Canada under authority of the Chairman of the Committee of the Privy Council on Scientific and Industrial Research. The *Canadian Journal of Research* is edited by a joint Editorial Board consisting of members of the National Research Council of Canada and the Royal Society of Canada.

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Canadian Journal of Research

Issued by THE NATIONAL RESEARCH COUNCIL OF CANADA

VOL. 22, SEC. E. JUNE, 1944 NUMBER 3

THE RELATIVE SWEETNESSES OF CERTAIN SUGARS, MIXTURES OF SUGARS, AND GLYCEROL[1]

BY A. T. CAMERON[2]

Abstract

The relative sweetnesses of the sugars glucose and lactose and of the alcohol glycerol, as compared with sucrose, vary with concentration.

The relative sweetness of glucose, or lactose, or glycerol, compared with either of the other two, does not change with concentration, within the limits of the experimental method used.

The following have been found to be equally sweet:

(*i*) 2.0% sucrose and 3.8% glucose; 10.0% sucrose and 14.7% glucose; 20.0% sucrose and 25.0% glucose.

(*ii*) 2.0% sucrose and 6.5% lactose; 5.0% sucrose and 14.9% lactose; 8.0% sucrose and 21.7% lactose.

(*iii*) 2.25% sucrose and 4.0% glycerol; 5.5% sucrose and 8.0% glycerol; 8.9% sucrose and 12.0% glycerol.

A method is described for calculating the sweetness of a mixture of sugars of known composition in terms of that of a specific concentration of sucrose or of glucose. The sweetness of each sugar is expressed in terms of that one of them for which the rate of change of the ratio of sweetness to concentration is least altered with changing concentration. The arithmetical sum of the values so calculated, referred to the appropriate curve of relative sweetness, gives the corresponding value of sucrose or glucose.

The accuracy of this method is demonstrated.

Introduction

In a recent paper (3) the earlier literature concerning sucrose, glucose, and fructose was dealt with, and experiments on these sugars were reported which led to the following conclusions:

(*i*) The majority of people lack a delicate taste sense for sweetness.

(*ii*) The relative sweetnesses of different sugars vary with concentration, and the sweetness of one sugar is apparently enhanced by the presence of a second sugar. (These findings confirmed the work of Dahlberg and Penczek (5).)

(*iii*) Alpha-dextroglucose is sweeter than beta-dextroglucose.

In the present paper results of comparisons of the sweetnesses of sucrose and lactose, and of sucrose and glycerol are reported, and in addition the results of studies of mixtures of certain sugars, and of sugars and glycerol. These have

[1] *Manuscript received April 12, 1944.*

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led to a simple method of calculating the sweetness of any such mixture in terms of that of a particular concentration of glucose or of sucrose, provided the concentration of each constituent of the mixture is known, and its curve of comparative sweetness against either glucose or sucrose has been determined.

There are but few statements in the literature concerning the sweetness of lactose. Paul (6), using 3% sucrose as standard, stated it to be 0.27 (i.e., presumably, 3% sucrose and 11% lactose have equal sweetness). Biester *et al.* (1), using the threshold value method, claimed that 1.3% sucrose and 8.1% lactose were equally sweet. Dahlberg and Penczek (5) found the following to be equally sweet (figures in percentages): sucrose 2.0, and lactose 6.0; sucrose 5.0, and lactose 13.1; sucrose 10.0, and lactose 20.7; sucrose 15.0, and lactose 27.8; sucrose 20.0, and lactose 33.3.

Still fewer measurements of the sweetness of glycerol have been recorded. Paul (6) stated that, compared with 3% sucrose, its sweetness was 0.48 (i.e., 3% sucrose and 6.25% glycerol were equally sweet). Carr, Beck, and Krantz (4), using the threshold method, stated that if sucrose is given the value 100, that for glycerol is 108. They did not state the actual concentration of sucrose. It has been shown that such threshold values apply only to threshold concentrations (3, 5). Using Biester's threshold value for sucrose, 1.3% (1), the corresponding concentration for glycerol would be 1.2%. But little stress can be laid on the work of Carr *et al.* They incidentally stated that alpha- and beta-glucose "have exactly the same degree of sweetness" (the value 75), while "the isomeric substances mannitol, sorbitol and dulcitol have approximately the same degree of sweetness" (assigning to them the respective values 57, 54, and 72). Obviously their method permitted only very approximate comparisons, when they themselves drew such conclusions. In this connection it is interesting to note that Brigl and Scheyer (2) found that derivatives of beta-glucose invariably have a bitterer taste than those of alpha-glucose.

In the earlier paper (3) comparisons of glucose and sucrose gave a curve that indicated that the sweetness of glucose at different concentrations was slightly less than that found by Dahlberg and Penczek. Two possible causes were suggested: (*i*) equilibrium alpha- and beta-glucose solutions were used throughout, whereas Dahlberg and Penczek may have used freshly made up solutions, predominantly alpha-glucose, and therefore sweeter, and (*ii*) untrained tasters were used, whose judgments may have been more affected by the additional tastes or flavours of the sugars than those of the trained tasters used by Dahlberg and Penczek. This potential source of error will be discussed later.

The apparent enhancement of sweetness of one compound by presence of another was first reported by Paul for mixtures of saccharine and dulcine, when compared with sucrose. He considered the effect as in reality merely additive. Dahlberg and Penczek showed that addition of glucose or corn syrup to sucrose solutions appeared to produce a much greater degree of

sweetness than the amounts added intrinsically possessed (as judged by direct comparison with sucrose solutions). This phenomenon has now been examined in some detail.

Experimental Results

Method of Measurement

A new first-year class of medical students was used as tasters for the work now reported. By the elimination test (3) 24 were selected out of 47 tested. Of the 24, two proved unreliable in their judgments and were almost immediately eliminated; two others subsequently became unavailable through illness. The proportion rejected was somewhat smaller than in the earlier elimination tests.

Some of the student tasters suggested that smoking might be the important factor lessening delicacy of taste perception. Enquiry was made of all the 47 as to whether they were non-smokers, occasional smokers, or habitual smokers. The results were:

Smokers:	selected, 4;	rejected, 7;	percentage selected, 36.
Occasional smokers:	selected, 2;	rejected, 7;	percentage selected, 22.
Non-smokers:	selected, 16;	rejected, 11;	percentage selected, 59.

While smoking is evidently a factor, it is obviously not the sole factor. (The large proportion of non-smokers selected was in part due to the large proportion of non-smokers in the whole group.)

It became evident, as the work proceeded, that the "tasters" improved in delicacy of perception.

The actual method of measurement has been fully described (3), and will be only briefly outlined here. The dairy-tasting method was used. Usually three solutions were compared, there being two concentrations of one sugar, and one of a second (or of glycerol). The two concentrations of the first sugar were so selected as to give a definitely perceptible difference of sweetness. The taster tasted the solutions (in roughly comparable amounts) in any order, and as often as he pleased. Each amount of solution was held in the mouth for approximately the same interval and then spat out. The taster was informed that two of the three, being different concentrations of the same sugar, must have a different sweetness, while the third might differ from both or be equal to one. All solutions were numbered, and the numbers scrambled, so that the taster had no clue as to which sugar was which. (For one or two exceptions to this rule in the later experiments, see the protocols.) He was asked to arrange the series in order of sweetness.

The number of tasters actually utilized in a single measurement (in the present series) varied from 14 to 21, tested in two groups on separate days. (Occasionally obviously wrong results had to be rejected, as when a taster reported for a set of three solutions that two different concentrations of the same sugar were equally sweet.)

The sweetness of a specific concentration of one sugar was measured in terms of a second by finding a concentration of the second that all the tasters

agreed was less sweet than the first, and then another concentration that all agreed was sweeter than the first. A series of intermediate concentrations were compared, successive concentrations differing by equal increments.

Throughout this paper the following abbreviations will be used where convenient: *S* for sucrose %; *G* for glucose %, *F* for fructose %; *L* for lactose %; *Gy* for glycerol %.

The method of calculation used in the earlier paper was wrong, although, fortunately, the errors arising from its use were negligible.

The data of the following example are taken from the earlier paper (3); the method of test is indicated, and a more accurate method of calculation employed.

Example of an Experiment—Comparison of 2% Sucrose with Glucose Solutions

Triads of solutions compared: 2*S*/3*G*/3.9*G*; 2*S*/3.3*G*/4.2*G*; 2*S*/3.6*G*/4.5*G*. Also compared: 2*S*/4.8*G*. The results with each triad gave comparisons between the sucrose solution and two concentrations of glucose. The "votes" of those reporting equality were halved between the two solutions concerned, and the resulting totals are shown in parentheses. Results were as follows:

Concentrations compared:	2*S* : 3*G*	2*S* : 3.3*G*	2*S* : 3.6*G*	2*S* : 3.9*G*
No. reporting *S* sweeter:	26 (100%)	16 (18) (75%)	11 (12½) (57%)	8 (14) (54%)
No. reporting *G* sweeter:	0 (0%)	4 (6) (25%)	8 (9½) (43%)	6 (12) (46%)
No. reporting equality:	0	4	3	12

Concentrations compared:	2*S* : 4.2*G*	2*S* : 4.5*G*	2*S* : 4.8*G*
No. reporting *S* sweeter:	3 (3½) (15%)	2 (9%)	0 (0%)
No. reporting *G* sweeter:	20 (20½) (85%)	21 (91%)	23 (100%)
No. reporting equality:	1	0	0

Calculation:

Glucose concn., %	Total no. of tasters, %	No. reporting sucrose sweeter, %
3.0	100	100
3.3	100	75
3.6	100	57
3.9	100	54
4.2	100	15
4.5	100	9
4.8	100	0
Difference = 1.8	Sum = 700	Sum = 310

$$310 \times 1.8/700 = 0.8$$
$$3.0 + 0.8 = 3.8$$

Hence 2% sucrose and 3.8% glucose are equally sweet.

Material Employed in the New Experiments

Sucrose: Redpath sugar cubes, 99.0 ± 1% pure (polarimeter test).
Acadia cubes, 99.7 ± 1% pure (polarimeter test).

Glucose: "Dextrosol" (a glucose hydrate preparation), 100 ± 1% pure (polarimeter test).

Lactose: Lactose hydrate, Mallinckrodt "Analytical reagent", giving a specific rotation (calculated as lactose) of 53.4° ± 0.6°.

Glycerol: Merck "Glycerin", U.S.P., c.p.

All results for glucose and for lactose are given in terms of the anhydrous compounds. All glucose solutions were prepared at least 16 hr. before use,

and were therefore equilibrium mixtures of alpha- and beta-dextroglucose. All lactose solutions also were so prepared, since it seemed probable that the corresponding two mutarotatory forms of lactose also might possess different sweetnesses; thus the sweetness of the lactose solutions measured is that of equilibrium mixtures. (The slow rate of solution of lactose at ordinary temperatures precluded any attempt to detect a difference of sweetness between the two forms.)

Solutions were generally used within 24 hr., and never when more than two days old. None showed any trace of mould growth. (Lactose solutions could not be used when much more than 24 hr. old.)

Experiments Already Reported

Since the results of the earlier paper (3) are used in this, they are given below, with corrected values, the experiments being numbered with Roman numerals. By contrast those now first reported are numbered with Arabic numerals. Also, since the calculations in the earlier paper were wrong, the protocols at the end of this paper include the earlier experiments.

Experiment I. Comparison of sucrose and glucose.

Results: 2% sucrose and 3.8% glucose are equally sweet.
10% sucrose and 14.7% glucose are equally sweet.
20% sucrose and 25.0% glucose are equally sweet.

Experiment II. Comparison of alpha-dextroglucose with the equilibrium mixture of the alpha- and beta-forms.

Result: The alpha-form is sweeter, by an undetermined amount.

Experiment III. "Enhancement effect."

Results: 15% sucrose is equal in sweetness to a mixture of 10% sucrose and 5.7% glucose.

Experiment IV. Comparison of sucrose and fructose.

Results: 5.0% sucrose and 4.6% fructose are equally sweet.
5.5% sucrose and 5.0% fructose are equally sweet.
17.8% sucrose and 15.0% fructose are equally sweet.

Comparison of Sucrose with Mixtures of Sucrose and Glucose

It was pointed out in the previous paper that when such mixtures are calculated in terms of sucrose there is an apparent enhancement in the sweetness of the added glucose, but that when the calculations are made in terms of glucose, the results are merely, and fairly correctly, additive. This seemed to merit closer examination. Experiment III was therefore repeated, using a much larger number of tasters.

Experiment 1. Determination of the amount of glucose needed to bring the sweetness of 10% sucrose equal to that of 15% sucrose.

Result: 5.5% glucose.

From the curve in Fig. 1 the sweetness of 15% sucrose equals that of 20.05% glucose, while those of 10% sucrose and 14.7% glucose are equal (cf. Experiment I). The difference, 5.35% glucose, is in close agreement with the figure found. Hence it seemed possible to calculate the needed quantity of glucose in such mixtures. This was checked and confirmed by the following two experiments.

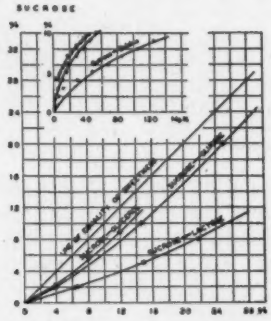

FIG. 1. *Curves showing the comparative sweetnesses of sucrose, glucose, lactose, and glycerol (from data in the paper). Also curves showing the comparative sweetnesses of sucrose, dulcine, and saccharine (from Paul's data).*

Experiment 2. Determination of X, in the sweetness equation

$$15S = 5S + XG.$$

By calculation from Fig. 1:

$15S$	$= 20.05G$
$5S$	$= 8.3G$
Difference	$11.75G$
Found	$11.8G$

Experiment 3. Determination of X in the sweetness equation

$$20S = 10S + XG.$$

By actual determination (Expt. I):

$20S$	$= 25.0G$
$10S$	$= 14.7G$
Difference	$10.3G$
Found	$10.15G$

Comparison of Sucrose and Equilibrium Mixtures of Lactose

Experiment 4. The following were found to be equally sweet:

2.0% sucrose and 6.5% lactose.
5.0% sucrose and 14.9% lactose.
8.0% sucrose and 21.7% lactose.

These results give a curve which is shown in Fig. 1.

Experiment 5. Determination of X in the sweetness equation

$$10S = 5S + XL$$

By calculation from Fig. 1:

$10S$	$= 25.5L$
$5S$	$= 14.9L$
Difference	$10.6L$
Found	$10.8L$

Comparison of Glucose and Lactose

No direct comparison has been made, but the respective comparisons with sucrose give values that are plotted in Fig. 2, to give a straight line within the limit of error. This is used in Experiment 6.

Experiment 6. Determination of X in the sweetness equation

$$10G = 5G + XL$$

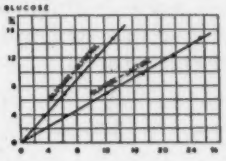

FIG. 2. *Curves showing the comparative sweetnesses of glucose, lactose, and glycerol.*

By calculation from Fig. 2:

$10G$	$= 17.7L$
$5G$	$= 8.85L$
Difference	$8.85L$
Found	$9.0L$

Calculation of the Sweetness of a Mixture of Sucrose, Glucose, and Lactose

From Figs. 1 and 2 the sweetness can be calculated in terms of either glucose or lactose, and then from Fig. 1 in terms of sucrose. The following is an example.

Experiment 7. Determination of X in the sweetness equation

$$XS = 2S + 5G + 10L$$

By calculation:

$2S$	$= 3.8G$	or	$2S$	$= 6.5L$
$5G$	$= 5.0G$		$5G$	$= 8.9L$
$10L$	$= 5.6G$		$10L$	$= 10.0L$
Total	$14.4G$		Total	$25.4L$
equal to	$9.8S$		equal to	$9.9S$
Found	$10.1S$		Found	$10.1S$

Comparison of Sucrose and Glycerol

This presented some difficulty on account of the extra taste (other than sweetness) of glycerol, its "bitterness" completely upsetting the judgments of some tasters, who either could make no comparison with sucrose, or whose conclusions were obviously wrong and had to be discarded.

Experiment 8. The following were found to be equally sweet:

4.0% glycerol and 2.25% sucrose.
8.0% glycerol and 5.5% sucrose.
12.0% glycerol and 8.9% sucrose.

The slightly smoothed curve is shown in Fig. 1.

Experiment 9. Determination of X in the sweetness equation

$$12Gy = 6Gy + XS$$

By calculation from Fig. 1:

(Difference) $6Gy = 3.8S$
Found $3.9S$

Comparison of Glucose and Glycerol

No direct comparison was made, but the respective comparisons with sucrose gave values which plotted to a straight line within the limit of error (cf. Fig. 2). This is used in Experiment 10.

Experiment 10. Determination of X in the sweetness equation

$$10Gy = 5Gy + XG.$$

By calculation from Fig. 2:

$10Gy = 11.0G$
$5Gy = 5.5G$
Difference $5.5G$
Found $5.3G$

Discussion of Results

Error of Measurement

No attempt has been made to estimate this. Two factors concerned are the number of tasters used, and the difference between successive increments of concentration. Probably a more important, but incalculable factor, is the effect of additional tastes or flavours possessed by different sweetening agents (cf. next section). Tables I and II suggest that the number of tasters is of more importance than the actual increment between successive concentrations.

TABLE I

COMPARISON OF THE RESULTS WITH THE ACTUAL INCREMENT OF CONCENTRATION USED, AND THOSE OBTAINED WITH TWICE THAT INCREMENT

Expt. No.	Actual increment	Actual result	Doubled increment	Result with doubled increment
I *A*	$0.3G$	$2S = 3.8G$	$0.6G$	$2S = 3.8G$
I *B*	$0.5G$	$10S = 14.7G$	$1.0G$	$10S = 14.8G$
IV *C*	$0.75S$	$15F = 17.8S$	$1.5S$	$15F = 17.7S$
1	$0.5G$	$15S = 10S + 5.5G$	$1.0G$	$15S = 10S + 5.5G$
4 *A*	$0.5L$	$2S = 6.5L$	$1.0L$	$2S = 6.5L$
4 *B*	$0.5L$	$5S = 14.9L$	$1.0L$	$5S = 14.9L$
7	$0.5S$	$10.1S$ = (Mixture)	$1.0S$	$10.1S$ = (Mixture)
8 *B*	$0.5S$	$8Gy = 5.5S$	$1.0S$	$8Gy = 5.65S$

TABLE II

COMPARISON OF RESULTS USING DIFFERENT NUMBERS OF TASTERS

Expt. No.	Group I		Group II		Groups I + II	
	No. of tasters	Result	No. of tasters	Result	No. of tasters	Result
		%		%		%
1	10 – 12	5.1	7 – 9	5.7	17 – 21	5.5
2	9 – 11	11.9	9	11.7	18 – 20	11.8
3	10	10.1	9	10.1	19	10.15
4 *A*	9 – 12	6.3	7 – 9	6.6	17 – 20	6.5
4 *B*	7 – 12	15.1	7 – 9	14.7	14 – 21	14.9
4 *C*	10 – 11	21.9	7 – 8	21.5	18 – 19	21.7
5	10	10.8	6 – 8	10.8	16 – 18	10.8
6	10 – 11	9.1	8	8.9	17 – 19	9.0
7	10	9.9	8	10.3	18	10.1
8 *A*	9 – 10	2.3	6 – 8	2.2	16 – 17	2.25
8 *B*	9 – 10	5.3	6 – 8	5.6	16 – 18	5.5
9	10	3.8	6	4.0	16	3.9
10	10	5.1	6	5.6	16	5.3

Apparently the use of 15 to 20 tasters permits reasonably accurate conclusions.

Additional Tastes or Flavours

It was pointed out in the earlier paper (3) that the various specific tastes or flavours possessed by sweetening agents in addition to sweetness often confuse some proportion of untrained tasters (especially those with delicate taste perception) thus leading to some degree of error in their conclusions about relative sweetness. Many, perhaps the majority of individuals, do not perceive the minor extra flavours (such as those distinguishing sucrose and glucose) yet to a minority glucose by comparison is "bitter" or "sour", while sucrose in weaker solution is "flat". Such descriptions, and those now to be mentioned, have been made when the identities of the sweetening agents were unknown to the tasters.

Some striking comments were made during the course of the present experiments. Comparison of lactose and sucrose solutions presented definite difficulties to a few tasters. Sucrose (5%) contrasted with lactose solutions of similar sweetness was reported as "bitter" or "peculiar" or "basic"; less sweet lactose solutions were "dull" by comparison.

Stronger solutions of lactose (20 to 25%) were "salt" or "sharp" to a number of tasters. One found them so "salt" that no comparison with sucrose was possible. Sucrose (8%) was definitely "bitter" to several, by comparison. One taster reported 24.5% lactose sweeter than 21.5% lactose, and this sweeter than 8% sucrose (calculation from all comparisons indicated that 8% sucrose and 21.7% lactose are equally sweet). He labelled the 24.5% lactose as "salt" and the 8% sucrose as "bitter".

Mixtures of lactose and sucrose still were "salt" to some tasters (and in one or two instances comparisons were not possible).

Glycerol proved even more embarrassing in a few cases. To most tasters, in the concentrations tested, it was bitter-sweet, although they could ignore the slightly bitter taste. Some were unable to do this. The same lady who could not make comparisons with strong lactose solutions was equally unable to make comparisons with 8 or 12% glycerol, describing the taste of the latter as resembling that of soybean sauce.

One taster found 12% glycerol sweeter than 12% sucrose, although 15 other tasters found 11% sucrose sweeter than the glycerol solution, and 14 of the 15 found 10% sucrose sweeter. The calculated result (excluding the anomalous comparison) was equality between 12% glycerol and 8.9% sucrose. One felt justified therefore in making this exclusion.

It is possible that the figures calculated for equality between solutions are slightly incorrect because of errors in judgment arising from the additional sensory effects, errors not great enough to be obvious and to justify exclusion of individual results. Thus the slopes of the curves in Fig. 1 may be slightly different from those for true values, although the type of curves is undoubtedly correct.

In the mixtures the extra sensations in most cases did not appear to cause difficulty in making comparisons. Errors should be proportionately less.

On the whole it seems reasonable to conclude that while the actual results reported in this paper may be no more than approximately accurate, yet the type of error affecting one set of results will affect others in similar fashion (and mixtures in an intermediate degree), so that all the results may be compared with each other.

Comparison with Earlier Results

As mentioned already, the difference between the results of Dahlberg and Penczek for sucrose and glucose, and those obtained in the present investigation could be attributed to (*i*) difference in experience of the tasters, especially in ignoring the extra sensations, and (*ii*) difference between solutions predominantly alpha-glucose, and those of equilibrium mixtures of glucose.

The sucrose–lactose curve of Fig. 1 differs in a similar manner from that of Dahlberg and Penczek. The same two causes probably explain the difference. The higher concentrations of lactose studied by Dahlberg and Penczek must have been supersaturated, and no attempt has been made to work with such solutions allowed to stand overnight in a cool room, since under such conditions solutions slightly above 25% were found to deposit crystals. The difficulty in obtaining rapid solution of lactose except at high temperatures precluded any attempt to demonstrate differences in sweetness between its two mutarotatory forms; such difference is very probable.

The two previously recorded figures for the sweetness of glycerol are in complete disagreement with each other; neither is close to the results now recorded.

Results with Sucrose, Glucose, Lactose, and Glycerol

The relative sweetness of glucose, lactose, or glycerol, as compared with sucrose, changes with change of concentration.

The relative sweetness of glucose, or lactose, or glycerol, compared with either of the other two, does not change with concentration, within the limits of the experimental method used. This is shown by contrasting the curves in Fig. 2 with those in Fig. 1.

Results with Mixtures

These are summarized in Table III, in which the actual experimental result is compared with results calculated from Figs. 1 and 2, equating all values in terms of sucrose, and of one or more of the other sweetening agents.

TABLE III

EXPERIMENTS WITH MIXTURES OF SUGARS, ETC.

Expt. No.	Actual result	Equated as sucrose	Equated as glucose	Equated as lactose	Equated as glycerol
1	$15S = 10S + 5.5G$	$15S = 13.0S$	$20.05G = 20.2G$	—	—
2	$15S = 5S + 11.8G$	$15S = 12.6S$	$20.05G = 20.1G$	—	—
3	$20S = 10S + 10.15G$	$20S = 16.35S$	$25.0G = 24.85G$	—	—
5	$10S = 5S + 10.8L$	$10S = 8.5S$	—	$25.5L = 25.7L$	—
6	$10G = 5G + 9.0L$	$6.2S = 6.6S$	$10.0G = 10.05G$	$17.6L = 17.8L$	—
7	$10.1S = 2S + 5G + 10L$	$10.1S = 7.9S$	$14.8G = 14.5G$	$25.75L = 25.3L$	—
9	$12Gy = 6Gy + 3.9S$	$8.9S = 7.7S$	—	—	$12Gy = 12.1\ Gy$
10	$10Gy = 5Gy + 5.3G$	$7.1S = 5.9S$	$11.05G = 10.8G$	—	$10Gy = 9.8\ Gy$

In terms of sucrose the "equations" in Table III are in complete disagreement, but in terms of glucose, or lactose, or glycerol they show extremely good agreement. It is therefore necessary to consider why sucrose cannot be taken as basis of comparison, while either one of the other three can be selected.

If we compare the concentrations of solutions at different levels of sweetness, taking as standards glucose solutions of 2.5, 5.0, and 10.0%, then the corresponding concentrations of sucrose (calculated from Fig. 1), and of dulcine and saccharine (calculated from curves in Fig. 1 based on Paul's data) are shown in Table IV, along with the corresponding concentrations of glycerol and lactose calculated from Fig. 2. The ratios (r) between successive concentrations of the same substance are given in parentheses.

No compound has yet been measured that gives, for the corresponding set of solutions, values of r less than 2.0. While values of r are equal for glucose, glycerol, and lactose, they steadily increase in the order glucose, sucrose, dulcine, saccharine.

Paul's data indicate that mixtures of saccharine and dulcine give additive sweetness, when expressed in terms of sucrose, but not when expressed in terms of saccharine and dulcine (6). Data as between saccharine and dulcine, or for mixtures of either with sucrose, are not available.

TABLE IV

RELATIVE RATIOS BETWEEN INCREASING CONCENTRATIONS OF SERIES OF EQUALLY SWEET SOLUTIONS

Glucose, %	Glycerol, %	Lactose, %	Sucrose, %	Dulcine, %	Saccharine, %
2.5	2.25	4.4	1.25	0.008	0.0020
5.0 (2.0)	4.5 (2.0)	8.8 (2.0)	2.7 (2.16)	0.020 (2.5)	0.0055 (2.75)
10.0 (2.0)	9.0 (2.0)	17.6 (2.0)	6.25 (2.3)	0.067 (3.35)	0.022 (4.0)

Thus it would appear that in order to calculate the sweetness of a mixture of two or more sweetening agents, the sweetness of each must be expressed in terms of that one for which r has the smallest value, or, more generally, for which the rate of change of the ratio of sweetness to concentration is least altered with changing concentration.

(The values found for an impure preparation of fructose in the earlier paper were in agreement with those of Dahlberg and Penczek for a preparation whose purity was not stated, and the nature of the sucrose–fructose curve (cf. 3) suggests that the corresponding values of r for fructose should be very slightly less than those for sucrose.)

Thus apparently the ratio r increases in the order (glucose = glycerol = lactose), fructose (?), sucrose, dulcine, saccharine. More accurate results may disprove the equality for glucose and lactose, but until such are available, and such disproof adduced, this order is not exactly that of increasing sweetness. Size of molecule does not control the result (sucrose and lactose are of equal molecular size). Since saccharine and dulcine are sweet compounds not utilized in the body, while sucrose is a sugar foreign to the animal organism but utilizable by it, and glucose is a physiological sugar present in the blood supply to the taste buds, one is tempted to hazard an explanation based on this relationship (that the taste buds are conditioned to glucose, rather than to sucrose). But lactose, also a physiological sugar, is not a normal blood constituent, and glycerol, though a physiological compound, is not present free in blood nor in most tissues.

No satisfactory explanation can be offered at present.

Since the actual degree of sweetness that is perceived following stimulation of taste buds by a solution of a sweetening agent is undoubtedly a function of the total number of molecules acting on the taste buds, it may be assumed with reasonable certainty that these molecules will be most efficient in very dilute solution, and that, with increasing concentration, there will be decreasing efficiency of the stimulant. Thus if the concentration is increased by equal increments the increments of sweetness should decrease for all sweet substances; doubling the concentration will not double the sweetness of any compound. Of the compounds that have been examined the degree of decrease is least for glucose, lactose, and glycerol, somewhat greater for sucrose, and

still greater for saccharine. Taste sensations cannot of course be actually measured.

But *if it be assumed* that the increments of sweetness for glucose, lactose, and glycerol are equal for successive equal increments of concentration, then it becomes possible to calculate the corresponding values for increments of sweetness of other sweetening agents. Thus 5% sucrose, 8.3% glucose, and 15 mg. % saccharine are equally sweet; 10% sucrose, 14.7% glucose, and 55 mg. % saccharine are equally sweet; 25% sucrose and 29.8% glucose are equally sweet. With the assumption made, the effect of doubling the concentration of the sucrose (from 5 to 10%) is to increase its sweetness by the ratio 14.7/8.3, i.e., 1.8; the effect of increasing its concentration five times (from 5 to 25%) is to increase its sweetness by the ratio 29.8/8.3, i.e., only 3.6 times. The effect of increasing the concentration of saccharine from 15 to 55 mg. % (3.7 times) is to increase its sweetness only 1.8 times.

Similar findings are shown in graphic form in Fig. 3, in which equal levels in the vertical columns represent equal sweetness, each block in a vertical column representing an increment of sweetness equal to that of the corresponding block in another vertical column, while the area of the block represents the increment of concentration. In addition, with the assumption that has been made, the blocks of sweetness of glucose, glycerol, and lactose become respectively of equal size throughout their columns.

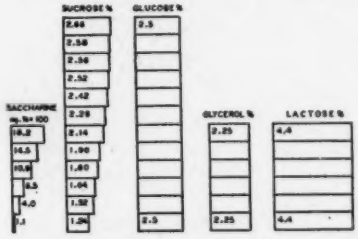

FIG. 3. *Schematic comparison of the relationship between sweetness and concentration of various sweetening agents.*

But the assumption is incorrect, and these blocks of sweetness should increase slightly in area with increasing height of column, while those for sucrose and and saccharine should increase even more than is shown in Fig. 3. Also it is possible to make the definite statement that the sweetness of 25% sucrose is *less* than 3.6 times that of 5% sucrose.

From Figs. 1 and 2 it is possible to construct iso-sweet curves for the various sugars, which can be used to calculate the sweetness of mixtures of known concentrations. Examples of such curves, for sucrose and glucose, are shown in Fig. 4, and the actual results found in Experiments 1, 2, and 3, inserted in the figure, are seen to approximate closely to the curves.

It is also now possible to determine mixtures of sucrose and glucose (in alpha- and beta-equilibrium) which will not only have equal sweetness, but

practically equal caloric value. Assuming the correctness of the results of this investigation (admittedly they may only be termed approximately correct, although, as far as most individuals can discern, indistinguishable

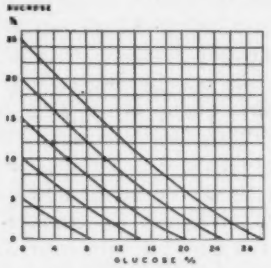

FIG. 4. *Iso-sweet curves for glucose and sucrose. All points on any one curve represent mixtures with equal sweetness. Values from Experiments 1, 2, and 3 indicated by crosses.*

from the true values, whatever these may be), and using the usually accepted caloric values for the two sugars (glucose, 3.74 Cal. per gm.; sucrose, 3.96 Cal. per gm.) examples such as the following can be calculated:

(1) The sweetness of 25% sucrose equals that of a mixture of 5.8% sucrose and 20.4% glucose. The energy value of a litre of 25% sucrose is 990 Cal. That of a litre of the mixture is (230 + 763 Cal. or) 993 Cal.

(2) The sweetness of 20% sucrose equals that of a mixture of 8.8% sucrose and 11.8% glucose. The energy value of a litre of 20% sucrose is 792 Cal. That of a litre of the mixture is (349 + 441 Cal. or) 790 Cal.

(3) The sweetness of 15% sucrose equals that of a mixture of 10% sucrose and 5.4% glucose. The energy value of a litre of 15% sucrose is 594 Cal. That of a litre of the mixture is (396 + 202 Cal. or) 598 Cal.

Acknowledgments

Thanks are due to Dr. F. D. White for making the various polarimetric determinations.

My colleague Professor N. R. Wilson has been kind enough to check the method of calculation used in this paper, and considers it reasonably adequate.

Thanks are due to the large number of students who, by acting as tasters, have made this investigation possible.

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Protocols of Experiments

The following additional abbreviations are used: concns. cpd., for concentrations compared; sucrose sweeter, for number reporting sucrose sweeter, etc.; equality, for number reporting equality; *M*, for mixture. The method of calculation has already been demonstrated (p. 48), and another example is given below (Experiment 1).

Expt. I (A). Glucose and 2% sucrose. See p. 48.

Expt. I (B). Glucose and 10% sucrose.

Concns. cpd.:	10*S*/13*G*	10*S*/13½*G*	10*S*/14*G*	10*S*/14½*G*
Sucrose sweeter:	13 (100%)	17 (19) (83%)	17 (17½) (76%)	9 (11½) (52%)
Glucose sweeter:	0 (0%)	1 (4) (17%)	5 (5½) (24%)	8 (10½) (48%)
Equality:	0	4	1	5

Concns. cpd.:	10*S*/15*G*	10*S*/15½*G*	10*S*/16*G*	10*S*/16½*G*
Sucrose sweeter:	9 (10½) (46%)	3 (3½) (15%)	1 (1½) (7%)	0 (0%)
Glucose sweeter:	11 (12½) (54%)	19 (19½) (85%)	20 (20½) (93%)	13 (100%)
Equality:	3	1	1	0

Expt. I (C). Glucose and 20% sucrose.

Concns. cpd.:	20*S*/21½*G*	20*S*/23*G*	20*S*/24½*G*	20*S*/26*G*
Sucrose sweeter:	16 (100%)	15 (15½) (97%)	10 (12) (67%)	4 (25%)
Glucose sweeter:	0 (0%)	0 (½) (3%)	4 (6) (33%)	12 (75%)
Equality:	0	1	4	0

Concns. cpd.:	20*S*/27½*G*
Sucrose sweeter:	0 (0%)
Glucose sweeter:	15 (100%)
Equality:	0

Expt. II. (For details see original paper (3).)

Expt. III. "Enhancement" effect.

Concns. cpd.:	15*S*/(10*S*+4½*G*)	15*S*/(10*S*+5½*G*)	15*S*/(10*S*+6½*G*)	15*S*/(10*S*+7½*G*)
Sucrose sweeter:	7 (100%)	3 (4) (57%)	0 (½) (7%)	0 (0%)
Glucose sweeter:	0 (0%)	2 (3) (43%)	6 (6½) (93%)	7 (100%)
Equality:	0	2	1	0

Expt: IV (A). Fructose and 5% sucrose.

Concns. cpd.:	5*S*/4*F*	5*S*/4.4*F*	5*S*/4.8*F*	5*S*/5.2*F*
Sucrose sweeter:	6 (100%)	3 (3½) (70%)	2 (2½) (42%)	0 (0%)
Glucose sweeter:	0 (0%)	1 (1½) (30%)	3 (3½) (58%)	5 (100%)
Equality:	0	1	1	0

Expt. IV (B). Sucrose and 5% fructose.

Concns. cpd.:	5*F*/4*S*	5*F*/4.8*S*	5*F*/5.6*S*	5*F*/6.4*S*
Fructose sweeter:	7 (100%)	7 (100%)	2 (29%)	0 (0%)
Sucrose sweeter:	0 (0%)	0 (0%)	5 (71%)	7 (100%)
Equality:	0	0	0	0

Expt. IV (C). Sucrose and 15% fructose.

Concns. cpd.:	15*F*/14½*S*	15*F*/15.25*S*	15*F*/16*S*	15*F*/16.75*S*
Fructose sweeter:	6 100%)	8 (100%)	4 (5) (71%)	5 (62½%)
Sucrose sweeter:	0 (0%)	0 (0%)	1 (2) (29%)	3 (37½%)
Equality:	0	0	2	0

Concns. cpd.:	15*F*/17½*S*	15*F*/18.25*S*	15*F*/19*S*	15*F*/19.75*S*
Fructose sweeter:	4 (67%)	5 (62½%)	2 (2½) (31%)	0 (0%)
Glucose sweeter:	2 (33%)	3 (37½%)	5 (5½) (69%)	8 (100%)
Equality:	0	0	1	0

Expt. 1. Determination of X in

$$15S = 10S + XG.$$

Triads:

$15S/(10S+3G)/(10S+6G)$; $15S/(10S+3\frac{1}{2}G)/(10S+6\frac{1}{2}G)$; $15S/(10S+4G)/(10S+7G)$; $15S/(10S+4\frac{1}{2}G)/(10S+7\frac{1}{2}G)$; $15S/(10S+5G)/(10S+8G)$; also $15S/(10S+5\frac{1}{2}G)$.

Concns. cpd.:	$15S/(10S+3G)$	$15S/(10S+3\frac{1}{2}G)$	$15S/(10S+4G)$	$15S/(10S+4\frac{1}{2}G)$
Sucrose sweeter:	18 (100%)	19 (19½) (97½%)	10 (12½) (73½%)	12 (14½) (72½%)
Mixture sweeter:	0 (0%)	0 (½) (2½%)	2 (4½) (26½%)	3 (5½) (27½%)
Equality:	0	1	5	5

Concns. cpd.:	$15S/(10S+5G)$	$15S/(10S+5\frac{1}{2}G)$	$15S/(10S+6G)$	$15S/(10S+6\frac{1}{2}G)$
Sucrose sweeter:	7 (11) (64½%)	6 (10½) (50%)	7 (10) (55½%)	5 (6) (30%)
Mixture sweeter:	2 (6) (35½%)	6 (10½) (50%)	5 (8) (44½%)	13 (14) (70%)
Equality:	8	9	6	2

Concns. cpd.:	$15S/(10S+7G)$	$15S/(10S+7\frac{1}{2}G)$	$15S/(10S+8G)$
Sucrose sweeter:	2 (3½) (10½%)	0 (1) (5%)	0 (0%)
Mixture sweeter:	12 (13½) (89½%)	18 (19) (95%)	17 (100%)
Equality:	3	2	0

Calculation:

$10S + 3.0G$	100%	100 %
$10S + 3.5G$	100%	97.5%
$10S + 4.0G$	100%	73.5%
$10S + 4.5G$	100%	72.5%
$10S + 5.0G$	100%	64.5%
$10S + 5.5G$	100%	50 %
$10S + 6.0G$	100%	55.5%
$10S + 6.5G$	100%	30 %
$10S + 7.0G$	100%	10.5%
$10S + 7.5G$	100%	5 %
$10S + 8.0G$	100%	0 %
Difference 5.0	Sum 1100	Sum 559

$$559 \times 5/1100 = 2.54$$
$$3 + 2.5 = 5.5$$

Hence $15S$ and $(10S + 5.5G)$ are equally sweet.

Expt. 2. Determination of X in

$$15S = 5S + XG.$$

Triads:

$15S/(5S+9G)/(5S+12G)$; $15S/(5S+10G)/(5S+13G)$; $15S/(5S+11G)/(5S+14G)$.

Concns. cpd.:	$15S/(5S+9G)$	$15S/(5S+10G)$	$15S/(5S+11G)$	$15S/(5S+12G)$
Sucrose sweeter:	19 (100%)	18 (90%)	10 (13) (72%)	8 (10½) (55%)
Mixture sweeter:	0 (0%)	2 (10%)	2 (5) (28%)	6 (8½) (45%)
Equality:	0	0	6	5

Concns. cpd.:	$15S/(5S+13G)$	$15S/(5S+14G)$
Sucrose sweeter:	2 (3½) (17½%)	0 (0%)
Mixture sweeter:	15 (16½) (82½%)	18 (100%)
Equality:	3	0

Expt. 3. Determination of X in

$$20S = 10S + XG.$$

Triads:

$20S/(10S+8G)/(10S+11G)$; $20S/(10S+9G)/(10S+12G)$; $20S/(10S+10G)/(10S+13G)$.

Concns. cpd.:	$20S/(10S+8G)$	$20S/(10S+9G)$	$20S/(10S+10G)$	$20S/(10S+11G)$
Sucrose sweeter:	19 (100%)	15 (16) (84%)	10 (11½) (60½%)	1 (1½) (8%)
Mixture sweeter:	0 (0%)	2 (3) (16%)	6 (7½) (39½%)	17 (17½) (92%)
Equality:	0	2	3	1

Concns. cpd.:	$20S/(10S+12G)$	$20S/(10S+13G)$
Sucrose sweeter:	1 (5½%)	0 (0%)
Mixture sweeter:	18 (94½%)	19 (100%)
Equality:	0	0

Expt. 4 (A). Comparison of lactose with 2% sucrose.

Triads:
2S/4½L/9½L; 2S/5L/7L; 2S/5½L/7½L; 2S/6L/8L; 2S/6½L/8½L.

Concns. cpd.:	2S/4½L	2S/5L	2S/5½L	2S/6L
Sucrose sweeter:	19 (100%)	18 (18½) (92½%)	12 (13½) (79%)	15 (16½) (82½%)
Lactose sweeter:	0 (0%)	1 (1½) (7½%)	2 (3½) (21%)	2 (3½) (17½%)
Equality:	0	1	3	3

Concns. cpd.:	2S/6½L	2S/7L	2S/7½L	2S/8L	2S/8½L
Sucrose sweeter:	7 (9½) (56%)	3 (5) (25%)	1 (2) (12%)	1 (5%)	0 (0%)
Lactose sweeter:	5 (7½) (44%)	13 (15) (75%)	14 (15) (88%)	19 (95%)	17 (100%)
Equality:	5	4	2	0	0

Expt. 4 (B). Comparison of lactose with 5% sucrose.

Triads:
5S/11L/14L; 5S/12L/15L; 5S/13L/16L; 5S/13½L/15½L; 5S/14L/17L; 5S/14½L/16½L.

Concns. cpd.:	5S/12L	5S/13L	5S/13½L	5S/14L	5S/14½L
Sucrose sweeter:	18 (100%)	21 (100%)	17 (17½) (92%)	8 (10) (56%)	8 (8½) (61%)
Lactose sweeter:	0 (0%)	0 (0%)	1 (1½) (8%)	6 (8) (44%)	5 (5½) (39%)
Equality:	0	0	1	4	1

Concns. cpd.:	5S/15L	5S/15½L	5S/16L*	5S/16½L	5S/17L
Sucrose sweeter:	8 (9) (50%)	5 (26%)	4 (5) (28%)	3 (21%)	0 (0%)
Lactose sweeter:	8 (9) (50%)	14 (74%)	12 (13) (72%)	11 (79%)	20 (100%)
Equality:	2	0	2	0	0

Expt. 4 (C). Comparison of lactose with 8% sucrose.

Triads:
8S/18½L/26L; 8S/20L/23L; 8S/21½L/24½L.

Concns. cpd.:	8S/18½L	8S/20L	8S/21½L	8S/23L
Sucrose sweeter:	18 (100%)	16 (16½) (87%)	8 (44%)	7 (7½) (39½%)
Lactose sweeter:	0 (0%)	2 (2½) (13%)	10 (56%)	11 (11½) (60½%)
Equality:	0	1	0	1

Concns. cpd.:	8S/24½L	8S/26L
Sucrose sweeter:	0 (0%)	0 (0%)
Lactose sweeter:	18 (100%)	17 (100%)
Equality:	0	0

Expt. 5. Determination of X in

$$10S = 5S + XL.$$

Triads:
10S/(5S+8½L)/(5S+11½L); 10S/(5S+9½L)/(5S+12½L); 10S/(5S+10½L)/(5S+13½L).

Concns. cpd.:	10S/(5S+8½L)	10S/(5S+9½L)	10S/(5S+10½L)	10S/(5S+11½L)
Sucrose sweeter:	18 (100%)	10 (10½) (65½%)	9 (9½) (59½%)	6 (33½%)
Mixture sweeter:	0 (0%)	5 (5½) (34½%)	6 (6½) (40½%)	12 (66½%)
Equality:	0	1	1	0

Concns. cpd.:	10S/(5S+12½L)	10S/(5S+13½L)
Sucrose sweeter:	2 (2½) (15½%)	0 (0%)
Mixture sweeter:	13 (13½) (84½%)	16 (100%)
Equality:	1	0

* *A group of five students was inadvertently omitted when this comparison was first made. Considerably later, when they were well trained, they were given 5S, 16L, 17L, and 18L to compare, being informed which solutions were sucrose, and which lactose, and the order of the latter, and asked to place the sucrose solution in its correct position with respect to the others. These results have been included, although, were they excluded, exactly the same result would be obtained.*

Expt. 6. Determination of X in

$$10G = 5G + XL.$$

Triads:

$10G/(5G+6\frac{1}{2}L)/(5G+9\frac{1}{2}L)$; $10G/(5G+7\frac{1}{2}L)/(5G+10\frac{1}{2}L)$; $10G/(5G+8\frac{1}{2}L)/(5G+11\frac{1}{2}L)$.

Concns. cpd.:	$10G/(5G+6\frac{1}{2}L)$	$10G/(5G+7\frac{1}{2}L)$	$10G/(5G+8\frac{1}{2}L)$	$10G/(5G+9\frac{1}{2}L)$
Glucose sweeter:	19 (100%)	17 (94%)	12 (13) (76½%)	7 (7½) (39½%)
Mixture sweeter:	0 (0%)	1 (6%)	3 (4) (23½%)	11 (11½) (60½%)
Equality:	0	0	2	1

Concns. cpd.:	$10G/(5G+10\frac{1}{2}L)$	$10G/(5G+11\frac{1}{2}L)$
Glucose sweeter:	0 (0%)	0 (0%)
Mixture sweeter:	18 (100%)	17 (100%)
Equality:	0	0

Expt. 7. Determination of X in

$$2S + 5G + 10L = XS.$$

Triads:

$M/8\frac{1}{2}S/10S$; $M/9S/10\frac{1}{2}S$; $M/9\frac{1}{2}S/11S$; also $M/8S/11\frac{1}{2}S$.

Concns. cpd.:	$M/8S$	$M/8\frac{1}{2}S$	$M/9S$	$M/9\frac{1}{2}S$
Mixture sweeter:	18 (100%)	18 (100%)	17 (17½) (97%)	14 (15) (83½%)
Sucrose sweeter:	0 (0%)	0 (0%)	0 (½) (3%)	2 (3) (16½%)
Equality:	0	0	1	2

Concns. cpd.:	$M/10S$	$M/10\frac{1}{2}S$	$M/11S$	$M/11\frac{1}{2}S$
Mixture sweeter:	8 (8½) (47%)	6 (6½) (36%)	1 (5½%)	0 (0%)
Sucrose sweeter:	9 (9½) (53%)	11 (11½) (64%)	17 (94½%)	18 (100%)
Equality:	1	1	0	0

Expt. 8 (A). Comparison of 4% glycerol and sucrose.

Triads:

$4Gy/1S/2S$ or $4Gy/1S/3S$; $4Gy/2S/4S$ or $4Gy/3S/4S$; $4Gy/1\frac{1}{2}S/2\frac{1}{2}S$.

Concns. cpd.:	$4Gy/1S$	$4Gy/1\frac{1}{2}S$	$4Gy/2S$	$4Gy/2\frac{1}{2}S$	$4Gy/3S$
Glycerol sweeter:	16 (100%)	16 (16½) (97%)	11 (12) (75%)	7 (41%)	0 (0%)
Sucrose sweeter:	0 (0%)	0 (½) (3%)	3 (4) (25%)	10 (59%)	16 (100%)
Equality:	0	1	2	0	0

Expt. 8 (B). Comparison of 8% glycerol and sucrose.

In this experiment the following triads were used: $8Gy/4S/6S$; $8Gy/5S/7S$. The tasters were not informed of the nature of the solutions, although most detected the glycerol solutions easily by their taste. Then in order to save time the now trained tasters were given $8Gy/4\frac{1}{2}S/5\frac{1}{2}S/6\frac{1}{2}S$, the glycerol solution being indicated, as well as the order of the sucrose solutions. They were told to place the glycerol solution in its correct order in relation to the others.

Concns. cpd.:	$8Gy/4S$	$8Gy/4\frac{1}{2}S$	$8Gy/5S$	$8Gy/5\frac{1}{2}S$
Glycerol sweeter:	18 (100%)	16 (100%)	11 (11½) (64%)	7 (8) (50%)
Sucrose sweeter:	0 (0%)	0 (0%)	6 (6½) (36%)	7 (8) (50%)
Equality:	0	0	1	2

Concns. cpd.:	$8Gy/6S$	$8Gy/6\frac{1}{2}S$	$8Gy/7S$
Glycerol sweeter:	3 (17%)	0 (½) (3%)	0 (0%)
Sucrose sweeter:	15 (83%)	15 (15½) (97%)	18 (100%)
Equality:	0	1	0

Expt. 8 (C). Comparison of 12% glycerol and sucrose. (Note the comment on p. 54 about this experiment.)

Triads:

$12Gy/7S/9S$; $12Gy/8S/10S$; for two or three students $12Gy/11S/12S$.

Concns. cpd.:	$12Gy/7S$	$12Gy/8S$	$12Gy/9S$	$12Gy/10S$	$12Gy/11S$
Glycerol sweeter:	15 (100%)	13 (87%)	7 (47%)	1 (7%)	0 (0%)
Sucrose sweeter:	0 (0%)	2 (13%)	8 (53%)	14 (93%)	(15) (100%)
Equality:	0	0	0	0	0

Expt. 9. Determination of X in

$$12Gy = 6Gy + XS.$$

Triads:

$12Gy/(6Gy+3S)/(6Gy+4\frac{1}{2}S)$; $12Gy/(6Gy+3\frac{1}{2}S)/(6Gy+5S)$;
$12Gy/(6Gy+4S)/(6Gy+5\frac{1}{2}S)$.

Concns. cpd.	$12Gy/(6Gy+3S)$	$12Gy/(6Gy+3\frac{1}{2}S)$	$12Gy/(6Gy+4S)$	$12Gy/(6Gy+4\frac{1}{2}S)$
Glycerol sweeter:	16 (100%)	9 (9½) (59½%)	6 (7½) (47%)	2 (3) (19%)
Mixture sweeter:	0 (0%)	6 (6½) (40½%)	7 (8½) (53%)	12 (13) (81%)
Equality:	0	1	3	2

Concns. cpd.	$12Gy/(6Gy+5S)$	$12Gy/(6Gy+5\frac{1}{2}S)$
Glycerol sweeter:	0 (0%)	0 (0%)
Sucrose sweeter:	16 (100%)	16 (100%)
Equality:	0	0

Expt. 10. Determination of X in

$$10Gy = 5Gy + XG.$$

Triads:

$10Gy/(5Gy+4\frac{1}{2}G)/(5Gy+6G)$; $10Gy/(5Gy+5G)/(5Gy+6\frac{1}{2}G)$;
$10Gy/(5Gy+5\frac{1}{2}G)/(5Gy+7G)$; $10Gy/(5Gy+4G)/(5Gy+5\frac{1}{2}G)$.

Concns. cpd.:	$10Gy/(5Gy+4G)$	$10Gy/(5Gy+4\frac{1}{2}G)$	$10Gy/(5Gy+5G)$	$10Gy/(5Gy+5\frac{1}{2}G)$
Glycerol sweeter:	16 (100%)	12 (13) (81%)	7 (8½) (53%)	7 (7½) (47%)
Mixture sweeter:	0 (0%)	2 (3) (19%)	6 (7½) (47%)	8 (8½) (53%)
Equality:	0	2	3	1

Concns. cpd.:	$10Gy/(5Gy+6G)$	$10Gy/(5Gy+6\frac{1}{2}G)$	$10Gy/(5Gy+7G)$
Glycerol sweeter:	4 (25%)	0 (0%)	0 (0%)
Mixture sweeter:	12 (75%)	16 (100%)	16 (100%)
Equality:	0	0	0

THE PHARMACOLOGICAL ACTIONS OF CAPAURINE[1]

By A. K. Reynolds[2] and R. A. Waud[3]

Abstract

The pharmacological actions of a new alkaloid, capaurine, and its O-methyl ether derivative have been studied. Capaurine was isolated from *Corydalis aurea*, a member of the plant family Fumariaceae, which is indigenous to Canada.

The base produces paralysis in frogs and convulsions in mice and rabbits, both effects being of central origin. The heart is depressed as is the smooth muscle of the intestine and uterus. Capaurine O-methyl ether is a convulsant drug exhibiting actions on the heart and smooth muscle quite similar to those of the alkaloid itself.

The alkaloids of fumariaceous plants have been the subject of an extensive chemical investigation by Manske (3) formerly of the National Research Council of Canada. The plant family Fumariaceae is closely related to the Papaveraceae, the source of the well-known opium alkaloids, and indeed Henry (2) has included the fumariaceous alkaloids along with those of the Papaveraceae. Manske has isolated over 30 new alkaloids from *Dicentra*, *Corydalis*, and *Adlumia* species. Capaurine, $C_{21}H_{27}O_5N$, was isolated from *Corydalis aurea*. Its chemical structure is not yet known but it is probably a base of the tetrahydroberberine type. It contains one phenolic hydroxyl and four methoxyl groups. It crystallizes in stout irregular prisms that melt sharply at 164° C.

Pharmacological studies of a number of fumariaceous alkaloids have been carried out by Waud (8, 9, 10) who investigated dicentrine, isocorydine, and corydine. Welch and Henderson (11) studied bicuculline, adlumine, and bicucine and Rice (5) investigated corlumine. Cularine was made the subject of a previous paper by one of us (A.K.R.) (4). The alkaloids of Chinese corydalis, or *Corydalis ambigua*, have been investigated by Chen *et al.* (1). Capaurine was briefly studied by Unna (7), the investigation being limited to a study of its action on intact frogs.

The capaurine for this study was generously supplied by Dr. Manske who also made available a quantity of its O-methyl ether derivative on which comparative studies were made on several preparations.

Experimental

Freshly prepared solutions of the hydrochloride were employed throughout the investigation. Doses for intact animals represent milligrams per kilogram.

[1] *Manuscript received April 12, 1944.*

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Frogs (winter)

Capaurine was injected into the lymph sac of frogs in doses ranging from 20 to 200 mg. Doses less than 100 mg. were without appreciable effect. Doses of 100 and 200 mg. were followed by marked respiratory depression and general descending paralysis. Electrical stimulation of the muscles and sciatic nerve produced normal responses, indicating that the paralysis produced by capaurine is of central rather than peripheral origin. These results were identical with those observed by Unna.

Capaurine O-methyl ether in doses of 200 mg. induced severe convulsions. Section of the sciatic nerve terminated the convulsive movements in the corresponding limb and destruction of the cord resulted in complete cessation of the seizures. The action of the methyl ether derivative on the intact frog is thus in sharp contrast to that of the base itself.

Mice

White mice received capaurine intraperitoneally in doses ranging from 50 to 200 mg. With the smaller doses there was a marked increase in respiratory rate and some retching, both symptoms probably indicating central stimulation. Following the administration of 100 mg. violent lashing convulsions occurred followed by periods of extreme exhaustion. Provided the animal did not die from asphyxia or exhaustion, recovery was usually complete. Violent convulsions were also produced by capaurine O-methyl ether in doses of 200 mg. This dose is twice the convulsive dose of capaurine.

Rabbits

The intraperitoneal administration of 125 mg. of capaurine to rabbits was followed by convulsions. There was severe opisthotonus and lashing about. The symptoms closely resembled those observed in mice. Subconvulsive doses appear to somewhat increase the pain threshold.

The Circulation

Perfusion of the frog heart (method of Howell and Cook).—Capaurine in concentrations of 1 : 100,000 and 1 : 50,000 and capaurine methyl ether in concentrations of 1 : 25,000 produced a marked increase in "tonus" accompanied by partial heart block. This action also occurred after atropine. The drugs appear to be depressant to cardiac muscle.

Perfusion of the frogs vessels.—Perfusion of the hind limbs of pithed frogs with both capaurine and capaurine methyl ether in concentrations ranging from 1 : 50,000 to 1 : 5000 gave no evidence of a change in calibre of the vessels.

Blood pressure.—Injected intravenously into rabbits under nembutal-ether anaesthesia in subconvulsive doses, capaurine produced a definite fall in carotid pressure followed by a gradual return to the normal level. This fall in blood pressure is no doubt a result of the cardiac depressant action of the drug.

Smooth Muscle Preparations

Intestine.—Spontaneously active segments of small intestine of the rabbit suspended in Locke solution were not affected by concentrations of less than 1 : 100,000. Concentrations of 1 : 50,000 and 1 : 25,000 produced rapid depression of rhythmic contractions. There was no change of rate or tonus. These concentrations of capaurine prevented the action of barium chloride. This action of capaurine is, apparently, directly on the smooth musculature.

Uterus.—Excised rat uteri suspended in Locke solution were not appreciably affected by capaurine or its derivative in concentrations up to 1 : 25,000. Concentrations of 1 : 10,000 produced a slight increase in tonus but a decrease in motility and rate.

Bronchi.—The isolated guinea pig bronchi, perfused according to the method of Thornton (6) showed no reaction to either capaurine or capaurine O-methyl ether.

Discussion

The action of capaurine on the intact animal is somewhat peculiar in that marked central nervous stimulation is produced in the mouse and rabbit, while central depression and paralysis is produced in the frog. In this respect it recalls the contrasting actions of morphine in the various animal species. The methyl ether derivative induced convulsions in all three animals, the convulsant dose being approximately twice that for capaurine.

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